REMARKS

Claim 1-48 are now in the application. Claims 1-42 are drawn to the elected invention. Claim 43-48 are drawn to non-elected invention and may be cancelled by the Examiner upon the allowance of the claims drawn to the elected invention.

Claim 1 has been amended to recite that the "purine is substituted at position 6 with a member selected from the group consisting of halogen, amino and protected amino." Support for this amendment can be found, for example, at page 4, lines 5 and 6 and page 8, lines 23-26. The amendments to the Claims do not introduce any new matter.

The rejection of Claims 1-42 under 35 U.S.C. 112, second paragraph, has been overcome by the amendment to Claim 1 and/or is not deemed tenable. In particular, Claim 1 and claims dependent therein recite that the substitution of position 6 is selected from the group consisting of halogen, amino acid, and protected amino. Independent Claim 20 as originally filed recited that the 6-substituted group "is selected from the group consisting of amino, protected amino, and alkoxy." Independent Claim 38 as originally filed recited that the 6-substituted group is amino or a protected amino. Independent Claim 40 as originally filed recited "6-azido." Accordingly, original Claims 20-42 were not indefinite and have not been amended.

Claims 1-42 were rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,821,357 to Chou et al. (hereinafter also "Chou") in view of U.S. Patent No. 5,180,824 to Bauman et al (hereinafter also "Bauman"). The cited references fail to render Claims 1-42 obvious.

Claims 1-42 relate to improved methods for synthesizing 2-chloro-9-(2-deoxy-2fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine [clofarabine] wherein the anionic form of a 2-chloro-6-substituted-purine is reacted with a protected and activated 2-deoxy-2-fluoro-D-arabinofuranose followed by reacting with an appropriate base such as ammonia to provide 2-chloro-9-(2-deoxy-2-fluro-β-D-arabinofuranosyl)-9*H*-purin-6-amine. The reported method for synthesizing 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine resulted in low overall yields of product, typically in the range of about 13%. Th described coupling reaction

producted a mixture of nucleosides from which the desired 9-β intermediate was obtained in only 32% yield after careful chromatography. Direct amination/deprotection of this material gave the desired 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine, plus a partially benzoylated 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine that required further base treatment. Pure 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine was obtained only after several recrystallizations to remove salts and residual benzamide.

Such inefficient reactions will inhibit the ability to commercially produce 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine. As discussed in the Specification, the present invention provides improved methods for synthesizing 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine that results in increased yields and/or reduced process steps.

Chou does not suggest or render obvious Claims 1-42 since, among other things, Chou does not relate to 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine. With respect to Claims 1-19 and 23, Chou fails to even remotely suggest a reaction of a purine nucleoside having a 6-alkoxy group to the desired final product. Likewise, Claim 39 and 42 which recite reacting with an alkali metal alkoxide provide a purine nucleoside having a 6-alkoxy group which in turn is reacted to provide the desired final product.

Furthermore, with respect to Claims 1-42, Chou differs from the present invention since, among other things, Chou does not even remotely suggest a starting purine having a chloro group in position 2. To include a chloro group in position 2 would be contrary to Chou which is explicitly concerned with purines having a fluoro group in position 2. For instance, see column 3, lines 29-54 thereof.

Bauman fails to overcome the above discussed deficiencies of Chou with respect to rendering obvious Claims 1-42. Bauman in contrast to the present invention, does not suggest preparing 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9*H*-purin-6-amine. Bauman is merely concerned with fludarabine and its phosphate. The reactants required by Bauman do not

include a purine having a chloro group in position 2. Furthermore, Bauman does not even remotely suggest a reaction of a purine nucleoside having a 6-alkoxy group to the desired product. For instance, see Claim 1-19, 23, 39, and 42.

Accordingly, even if Bauman were combined with Chou, the present invention would still not be suggested.

The mere fact that cited art may be modified in the manner suggested by the Examiner does not make this modification obvious, unless the cited are suggest the desirability of the modification. No such suggestion appears in the cited art in this matter. The Examiner's attention is kindly directed to In re Lee 61 USPQ2d 1430 (Fed. Cir. 2002) In re Dembiczak et al. 50 USPQ2d. 1614 (Fed.Cir. 1999), In re Gordon, 221 USPQ 1125(Fed. Cir. 1984), In re Lasowski, 10 USPQ2d. 1397 (Fed. Cir. 1989) and In re Fritch, 23, USPQ2d. 1780 (Fed. Cir. 1992).

In Dembiczak et al., supra, the Court at 1617 stated: "Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references. See, e.g., C.R. Bard, Inc., v. M3 Sys., Inc., 157 F.3d. 1340, 1352, 48 USPQ2d. 1225, 1232 (Fed. Cir. 1998) (describing 'teaching or suggestion motivation [to combine]' as in 'essential evidentiary component of an obviousness holding'), In re Rouffet, 149 F.3d 1350, 1359, 47 USPQ2d. 1453, 1459 (Fed. Cir. 1998) ('the Board must identify specifically...the reasons one of ordinary skill in the art would have been motivated to select the references and combine them');..."

Also, the cited art lacks the necessary direction or incentive to those or ordinary skill in the art to render the rejection under 35 USC 103 sustainable. The cited art fails to provide the degree of predictability of success of achieving the results attainable by the present invention needed to sustain a rejection under 35 USC 103. See Diversitech Corp. v. Century Steps, Inc. 7 USPQ2d 1315 (Fed. Cir. 1988), In re Mercier, 185 USPQ 74 (CCPA 1975) and In re Naylor, 152 USPQ 106 (CCPA 1966).

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Moreover, the properties of the subject matter and results which are inherent in the claimed subject matter and disclosed in the specification are to be considered when evaluating the question of obviousness under 35 USC 103. See Gillette Co. v. S.C. Johnson & Son, Inc., 16 USPQ2d. 1923 (Fed.Cir. 1990), In re Antonie, 195, USPQ 6 (CCPA 1977), In re Estes, 164 USPQ 519 (CCPA 1970), and In re Papesche, 137 USPQ 43 (CCPA 1963).

No property or result can be ignored in determining patentability and comparing the claimed invention to the cited art. Along these lines, see In re Papesch, supra, In re Burt et al, 148 USPQ 548 (CCPA 1966), In re Ward, 141 USPQ 227 (CCPA 1964), and In re Cescon, 177 USPQ 264 (CCPA 1973).

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

In the event the Examiner believes an interview might serve to advance the prosecution of this application in any way, the undersigned attorney is available at the telephone number noted below.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 22-0185, under Order No. 21381-00067-US from which the undersigned is authorized to draw.

Dated: December 16, 2003
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Respectfully submitted,

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